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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/436,892	11/09/1999	RUSSELL M. MEDFORD	04676.105045	7272

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EXAMINER

GABEL, GAILENE

ART UNIT

PAPER NUMBER

1641

DATE MAILED: 06/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/436,892	MEDFORD ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 08 April 2004.  
 2a) This action is FINAL.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-27,29-32 and 35-41 is/are pending in the application.  
 4a) Of the above claim(s) 7,8,11-14,16-20 and 37-39 is/are withdrawn from consideration.  
 5) Claim(s) 15,31,32,35 and 36 is/are allowed.  
 6) Claim(s) 1-6,9,10,21-27,29,30,40 and 41 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) 1-27,29-32 and 35-41 are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|  | 6) <input type="checkbox"/> Other: _____                                    |

## DETAILED ACTION

### ***Amendment Entry***

1. Applicant's amendment and response filed 4/6/04 is acknowledged and has been entered. Claims 1, 6, and 40 have been amended. Claims 1-27, 29-32, and 35-41 are pending.

In light of Applicant's argument, the withdrawal of claims 9 and 29 from consideration as claims drawn to non-elected invention, has been removed. Accordingly, claims 9 and 29 are rejoined with claims currently under prosecution. Claims 7, 8, 11-14, 16-20, and 37-39 remain withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Claims 1-6, 9, 10, 15, 21-27, 29-32, 35, 36, and 40-41 are under examination.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 9, 29, 40 and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9, step iv) is vague and indefinite because it is unclear how the addition of a third antibody, having a label attached thereto, detects the second antibody in step iii)

which binds to the combination in step ii). Does Applicant intend for the labeled antibody to bind an element within the combination in step ii) or that in step iii).

Claim 40, step iii) is vague and indefinite because it is unclear how adding the second antibody, having a label attached thereto, detects the combination in step ii). Does Applicant intend for the labeled antibody to bind an element within the combination in step ii).

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The claims are drawn to a method wherein a compound is administered to a human host to enhance clearing of cholesterol-containing low density lipoproteins, from here on CC-LDL. The CC-LDL is isolated from the host and is determined for a change in the three dimensional conformation of the lipoprotein, wherein a change in the three dimensional conformation of the lipoprotein is detected by antibody binding to a specific epitope of the lipoprotein, i.e. apoB-100, which subsequently binds the LDL receptor. The claimed invention purports this mechanism to enhancing the clearance of LDL. At page 14 of the specification, the compounds are identified as monosuccinic acid esters of probucol. Accordingly,

3. Claims 1-3, 6, 22-24, and 30 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Somers (US 6,121,319) for reasons of record.

Specifically in Examples 5 and 8, Somers assesses the effect of a compound, i.e. monosuccinic ester of probucol, on cholesterol in plasma of lipid-fed animals by 1) administering the compound (monosuccinic ester of probucol) to a host (rabbits) fed with high fat and high cholesterol diet and 2) determining and separating lipoprotein fractions from the rabbit plasma by fast phase chromatography, then analyzing for cholesterol and lipoprotein content; thus, observing for effects on total cholesterol and cholesterol containing lipoproteins, i.e. LDL, VLDL, and HDL (CC-LDL) clearance. Somers found that the monosuccinic acid esters of probucol resulted in statistically significant reduction (clearing) in total cholesterol and CC-LDL. According to Somers, chylomicrons, VLDL, and LDL participate in the transport of cholesterol between other peripheral tissues, i.e. intestinal and adipose, and liver (hepatic LDL receptors).

Specifically, VLDL and LDL transports cholesterol from liver to other peripheral tissues, i.e. LDL receptors.

Somers is silent in teaching that binding occurs between the compound (consisting of monosuccinic esters of probucol) and CC-LDL; thus resulting to a change in binding affinity of CC-LDL to LDL receptors.

However, the instant claims which recite "binding of the compound to LDL which enhances LDL clearance after subsequent binding to the LDL receptor", merely provide a newly discovered mechanism of a known compound which is monosuccinic acid ester of probucol, and therapeutic method use, thereof, wherein enhanced clearing of LDL subsequently results. Specifically, newly discovered mechanisms of known processes directed to the same purpose are not patentable because such results are inherent. The claim language is only a statement of purpose and intended result. The expression does not result in a manipulative difference in the steps of the claims.

Additionally, "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art. However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old known composition patentably new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art". Atlas Powder Co. v. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

4. Claims 4, 5, 10, 21, and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Somers (US 6,121,319) in view of Koren et al. (US 6,107,045) for reasons of record.

### ***Response to Arguments***

5. Applicant's arguments filed 4/8/04 have been fully considered but they are not persuasive.

A) Applicant argues that Somers does not disclose the presently claimed assays which are drawn to methods to assess whether a compound increases the binding affinity of a LDL to a LDL-receptor, potentially by causing a change in Apo B-100; thus, increasing the clearance of the LDL. According to Applicant, the references do not teach the claimed invention which discloses that certain compounds change the conformation of Apo B100 and increase the binding of certain types of LDL to LDL receptors.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., assays for determining the change in conformation of Apo B-100, to assess binding of a compound to CC-LDL and subsequent increase in binding affinity between CC-LDL and LDL receptor) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

B) Applicant argues that the combination of Somers with Koren does not suggest that the mechanism or binding activity of a compound on certain types of LDL to LDL receptors can be used to test whether compounds are effective in enhancing LDL clearance.

In response, the instant claims which recite "binding of the compound to LDL which enhances LDL clearance after subsequent binding to the LDL receptor", merely provide a newly discovered mechanism of a known compound which is monosuccinic acid ester of probucol, and therapeutic method use, thereof, wherein enhanced clearing of LDL subsequently results. Specifically, newly discovered mechanisms of known processes directed to the same purpose are not patentable because such results are inherent. The claim language is only a statement of purpose and intended result. The expression does not result in a manipulative difference in the steps of the claims. Specifically, the claims as recited are limited to determining whether binding occurred between the compound and the CC-LDL, by virtue of a resulting change, i.e. increase, in the binding affinity of the CC-LDL and LDL receptor (mechanism), which appears to be only manifested by the enhancement of the clearing of CC-LDL (end result = CC-LDL content). It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure.

Accordingly, the teaching of Somers as discussed supra reads on the rejected claims.

While the prior art disclosure may be silent as to the mechanism of the

compound to increase the binding affinity of CC-LDL to LDL receptor, the instant claims merely recite a newly discovered mechanism to obtain a same result in a method wherein a compound is assessed for its capacity to enhance clearance of CC-LDL. As pointed out previously, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Even though applicant has proposed or claimed the mechanism by which the compound functions, it does not appear to distinguish the prior art teaching; the same or nearly the same methods achieve the same end result. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

***Allowable Subject Matter***

6. Claims 15, 31, 32, 35, and 36 are allowable. Claims 9, 29, 40 and 41 would be allowable if rewritten or amended to overcome the rejections under 35 U.S.C. 112, second paragraph, set forth in this Office action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703)

305-0807. The examiner can normally be reached on Monday, Tuesday, and Thursday, 5:30 AM to 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-0169.



CHRISTOPHER L. CHIN  
PRIMARY EXAMINER  
GROUP 1800/1641

Gailene R. Gabel  
Patent Examiner  
Art Unit 1641  
June 16, 2004 *gk*